UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/811,593	03/29/2004	Muhammad Anzar	MTC 2002.1 (37-21 (53264)	2857

321 7590 08/28/2006

SENNIGER POWERS
ONE METROPOLITAN SQUARE
16TH FLOOR
ST LOUIS, MO 63102

EXAMINER	
GOUGH, TIFFANY MAUREEN	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 08/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/811,593	ANZAR ET AL.	
	Examiner	Art Unit	
	Tiffany M. Gough	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/3/06,9/22/06,11/5/06*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claims 18 and 19 are objected to because of the following informalities: Claim 18 states "...to form a buffered bye solution..." For examination purposes it has been interpreted as "...a dye solution..." Claim 19 states, " combining the a ..." For examination purposes it has been interpreted as "...a quencher..."

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-17,19,20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al (WO 02/043574, 6/6/2002 also published as PGPub US2004/0049801 A1) or Johnson (US 5,135,759) in view of D'Occhio (Animal Breeding, Use of New Technology, 1999).

Applicant claims a process for staining sperm cells comprising a staining mixture of sperm cells and a DNA fluorescent dye and further subjecting the mixture to temperatures in excess of 40°C. The mixture is subjected to the temperature for a sufficient amount of time to allow the dye to bind to the DNA. The desired period of time is from about 1-160 minutes and the dye concentration is from about 0.1-1000 μM. Applicant further claims adding a quencher to the staining mixture such as FD&C #40 and propidium iodide

Seidel et al disclose a method of staining sperm cells comprising a incubating sperm cells in a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentration greater than 40 μM at temperatures between about 30°C and about 40°C for a time between 50-200 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations. (see claims, 0035,0036 and 0037).

Johnson discloses disclose a method of staining cells comprising staining sperm cells in a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentrations ranging from 4-5μg/ml at temperatures between about 30°C and about 39°C for a time between 60-120 minutes, and further disclose optimizing these

parameters by adjusting time, temperature and dye concentrations(see column 4, lines 27-44).

Neither Seidel or Johnson teach the use of propidium iodide (PI) as a quencher in a staining mixture.

D'Occhio discloses a staining mixture comprising sperm in a semen buffer which is further incubated with Hoechst 33342 and propidium iodide (PI), i.e. a quencher, at temperatures of 32-35°C for 45-60 minutes (see p.252 first paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have added propidium iodide (PI) to a sperm staining mixture because D'Occhio teaches that PI quenches the fluorescence of Hoechst 33342, i.e. a DNA fluorescent dye, and only penetrates dead sperm (see p.252, first paragraph).

One of ordinary skill in the art would have been motivated to add a quencher such as PI because D'Occhio teaches PI as a quencher in a sperm staining mixture which is desirable because it quenches the fluorescence of Hoechst 33342 and only penetrates dead sperm which is beneficial during the sorting process (see p.252, first paragraph). One would reasonably have expected success in using PI as a quencher because it is known in the art as a quencher in staining mixtures comprising sperm and a DNA fluorescent dye.

Neither reference teaches incubating the staining mixture at temperatures exceeding 40°C for less than 30 minutes.

However, generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."). See MPEP 2144.05.

Claims 1-17,19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al (WO 02/043574, 6/62002 also published as PGPub US2004/0049801 A1) or Johnson (US 5,135,759) in view of Guthrie et al (Molecular Reproduction and Development, vol 61, 2002)

Applicant claims a process for staining sperm cells comprising a staining mixture of sperm cells and a DNA fluorescent dye and further subjecting the mixture to temperatures in excess of 40°C. The mixture is subjected to the temperature for a

sufficient amount of time to allow the dye to bind to the DNA. The desired period of time is from about 1-160 minutes and the dye concentration is from about 0.1-1000 μM. Applicant further claims adding a quencher to the staining mixture such as FD&C #40 and propidium iodide.

Seidel et al disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentration greater than 40 μM at temperatures between about 30°C and about 40°C for a time between 50-200 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations. (see 0035,0036 and 0037).

Johnson discloses disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentrations ranging from 4-5μg/ml at temperatures between about 30°C and about 39°C for a time between 60-120 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations (see column 4, lines 27-44).

Niether Seidel or Johnson teach the use of a quencher in combination with their staining mixture, specifically FD&C#40 in combination with the dye Hoechst 33342.

Guthrie et al teach a staining mixture comprising a buffered sperm mixture, sperm in BTS, which is further treated with Hoechst 33342 and FD&C 40. FD&C#40 is added to quench the fluorescence of Hoechst 33342 in dead sperm to differentiate them from the living sperm in the sample (see p.88 Material and Methods section).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have added FD&C#40 to a sperm staining mixture because Gunthrie teaches FD&C#40 to quench the fluorescence of Hoechst 33342, i.e. a DNA fluorescent dye, and to differentiate between living and dead sperm cells.

One of ordinary skill in the art would have been motivated to add a quencher such as FD&C#40l because Gunthrie teaches FD&C#40 as a quencher in a sperm staining mixture which is desirable because it quenches the fluorescence of Hoechst 33342 and only penetrates dead sperm which is known in the art to beneficial during the sorting process. One would reasonably have expected success in using FD&C#40 as a quencher because it is known in the art as a quencher in staining mixtures comprising sperm and a DNA fluorescent dye.

Claims 1-20 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al (WO 02/043574, 6/62002 also published as PGPub US2004/0049801 A1) or Johnson (US 5,135,759) in view of Garner et al (Biology of Reproduction, vol 53, 1995)

Applicant claims a process for staining sperm cells comprising a staining mixture of sperm cells and a DNA fluorescent dye and further subjecting the mixture to temperatures in excess of 40°C. The mixture is subjected to the temperature for a sufficient amount of time to allow the dye to bind to the DNA. The desired period of time is from about 1-160 minutes and the dye concentration is from about 0.1-1000 μM.

Applicant further claims adding a quencher to the staining mixture such as FD&C #40 and propidium iodide.

Seidel et al disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentration greater than 40 μM at temperatures between about 30°C and about 40°C for a time between 50-200 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations. (see 0035,0036 and 0037).

Johnson discloses disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentrations ranging from 4-5μg/ml at temperatures between about 30°C and about 39°C for a time between 60-120 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations (see column 4, lines 27-44).

Niether Seidel or Johnson teach the use of a quencher in combination with their staining mixture, specifically propidium iodide in combination with the dye SYBR-14.

Garner et al teach the staining of sperm cells with SYBR-14 and propidium iodide, which is useful in determining the proportions of living and dead sperm cells in sperm samples (see introduction first paragraph). They teach the preparation of a dye buffered solution which is then added to a buffered sperm solution to stain the sperm cells (see Material and Methods section, specifically paragraphs 6-9).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have added propidium iodide to a sperm staining mixture

because Garner teaches that as sperm die, they lose their ability to resist the influx of PI, which upon entering the sperm it quenches the SYBR-14 staining. They also note that a similar effect was also seen when used in combination with with Hoechst 33342 (see Discussion section).

One of ordinary skill in the art would have been motivated to add a quencher such as propidium iodide because Garner teaches PI as a quencher in a sperm staining mixture which is desirable because it quenches the fluorescence of SYBR-14 and Hoechst 33342. One would reasonably have expected success in using PI as a quencher because it is known in the art as a quencher in staining mixtures comprising sperm and a DNA fluorescent dye.

Claims 1-15,24-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al (WO 02/043574, 6/62002 also published as PGPub US2004/0049801 A1) or Johnson (US 5,135,759) in view of Van Demark et al (US 3,005,756,1961) or Salisbury et al (Journal of Reprod. Fertility vol. 6, 1953).

Applicant claims a process for staining sperm cells comprising a staining mixture of sperm cells and a DNA fluorescent dye and further subjecting the mixture to temperatures in excess of 40°C. The mixture is subjected to the temperature for a sufficient amount of time to allow the dye to bind to the DNA. The desired period of time is from about 1-160 minutes and the dye concentration is from about 0.1-1000 μM. Applicant further claims a staining mixture comprising a carbonate buffer comprising

0.097 moles/L of $NaHCO_3$, 0.173 moles/L of $KHCO_3$ and 0.090 moles/L of $C_6H_8O_7 \cdot H_2O$ in water, which inhibits sperm motility.

Seidel et al disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentration greater than 40 μM at temperatures between about 30°C and about 40°C for a time between 50-200 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations. (see 0035,0036 and 0037).

Johnson discloses disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentrations ranging from 4-5μg/ml at temperatures between about 30°C and about 39°C for a time between 60-120 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations (see column 4, lines 27-44).

None of the references teach the composition to further comprise 0.097 moles/L of $NaHCO_3$, 0.173 moles/L of $KHCO_3$ and 0.090 moles/L of $C_6H_8O_7 \cdot H_2O$ in water.

However, Van Demark et al (US 3,005,756,1961) disclose the use of an inhibitory diluent containing $NaHCO_3$,$KHCO_3$ and $C_6H_8O_7 \cdot H_2O$ in water (see col. 5, lines 55-75).

Salisbury et al (Journal of Reprod. Fertility vol. 6, 1953) teach the use of a buffer which inhibits sperm motility. The buffers contain $NaHCO_3$,$KHCO_3$ and $C_6H_8O_7 \cdot H_2O$ in

water (see p.352 Materials and Methods section), which are useful in determining which substrates are useful in the metabolism of spermatozoa (see p.352 1st full paragraph).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was made to use such a motility inhibitory buffer claimed by Van Demark or Salisbury, in combination with the staining mixture because such buffer is discloses as being useful in examining the which substrates are beneficial for spermatozoal metabolism and economy.

One of ordinary skill in the art would have been motivated to add such carbonate buffers to a sperm containing composition because as stated above, they are beneficial for examining useful substrates. One would reasonably have expected success in inhibiting sperm motility using such buffers because both Van Demark and Salibury teach these components to have an inhibitory effect.

Neither Van Demark nor Salisbury teach the exact amounts of each components as those claimed by applicant.

However, it would be obvious to one of ordinary skill in the art at the time of the invention to adjust the buffer components to a concentration optimal for such invention, therefore optimizing these result effective variables is the result of routine experimentation.

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or

workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference
process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."). See MPEP 2144.05

Claims 1-15,29-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al (WO 02/043574, 6/62002 also published as PGPub US2004/0049801 A1) or Johnson (US 5,135,759) in view of Sabuer et al (Journal of Reproduction and Fertility, vol 20, 2000) or De Pauw et al (Biology of Reproduction vol 67, 2002) in further view of Bruemmer et al (Journal of Animal Science, vol 80, 2002).

Applicant claims a process for staining sperm cells comprising a staining mixture of sperm cells and a DNA fluorescent dye and further subjecting the mixture to temperatures in excess of 40°C. The mixture is subjected to the temperature for a sufficient amount of time to allow the dye to bind to the DNA. The desired period of time is from about 1-160 minutes and the dye concentration is from about 0.1-1000 μM.

Applicant further claims the process to include a composition comprising a composition which regulates oxidation/reduction reactions such as pyruvate in amounts ranging from about 0.5μM to 50mM.

Seidel et al disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentration greater than 40 μM at temperatures between about 30°C and about 40°C for a time between 50-200 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations. (see 0035,0036 and 0037).

Johnson discloses disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentrations ranging from 4-5μg/ml at temperatures between about 30°C and about 39°C for a time between 60-120 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations (see column 4, lines 27-44).

Neither Seidel or Johnson teach the staining mixture to contain a composition which regulates oxidation/reduction reactions such as pyruvate.

However, Sabeur teach a composition comprising spermatozoa in TALP buffer , i.e. pyruvate, and Hoechst 33258, i.e. a DNA selective dye (see p.136, material and methods section). TALP media is known in the art to contain pyruvate at amounts greater than 50μM. For support, see IVF protocols at http://www.specialtymedia.com/05Resources/Protovols/ivfprotocol.htm. It is disclosed that TALP contains pyruvate in amounts of 0.5,1 and 2 ml, thus greater than 50μM.

De Pauw teach a composition comprising spermatozoa in TALP buffer, i.e pyruvate and SYBR-14, i.e. a DNA selective dye (see Materials and Methods section and p.10762nd full paragraph). TALP media is known in the art to contain pyruvate at amounts greater than 50μM. For support, see IVF protocols at http://www.specialtymedia.com/05Resources/Protovols/ivfprotocol.htm. It is disclosed that TALP contains pyruvate in amounts of 0.5,1 and 2 ml, thus greater than 50μM.

None of the references teach the composition to contain pyruvate at concentrations selected from 2.5,10,15,25 or 50 mM.

However, Bruemmer teaches the addition of pyruvate to sperm compositions in the amount of up to 10mM, but more preferable is the addition of between 2 to 5 mM of pyruvate. They teach that the addition of pyruvate to sperm compositions is beneficial because it maintains spermatozoal motion, it acts as an energy substrate and further (at high concentrations) acts as an antioxidant for spermatozoa (see p. 17,1st,2nd and 4th paragraphs).

It would have been obvious to one of ordinary skill in the art at the time of the invention was made to add pyruvate, at the claimed concentrations, to a sperm

composition because Bruemmer teaches the addition of pyruvate, in amounts of 2 to 10 mM, to a sperm composition to be beneficial because it maintains spermatozoal motion, acts as an energy substrate and further (at high concentrations) acts as an antioxidant for spermatozoa (see p. 17,1st,2nd and 4th paragraphs).

Therefore, one of ordinary skill in the art would have been motivated to make such a modification to a sperm containing composition because such concentrations are disclosed as being beneficial to sperm and therefore, one would reasonably have expected success in making a sperm composition comprising the claimed amounts of pyruvate as suggested by Bruemmer.

It would be obvious to one of ordinary skill in the art at the time of the invention to adjust the buffer components to a concentration optimal for such invention, therefore optimizing these result effective variables is the result of routine experimentation.

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference

process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."). See MPEP 2144.05.

Claims 1,29,30,31,35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel et al (WO 02/043574, 6/62002 also published as PGPub US2004/0049801 A1) or Johnson (US 5,135,759) in view of Remington (WO 02/077011 also US7015310 B2).

Applicant claims a process for staining sperm cells comprising a staining mixture of sperm cells and a DNA fluorescent dye and further subjecting the mixture to temperatures in excess of 40°C. The mixture further comprisies a composition which regulates oxidation/reduction reactions intracellularly or extracelllularly. The composition is selected from the group consisting of vitamin K and lipoic acid in amounts ranging from 1-100μM to 0.1-1.0mM respectively.

Seidel et al disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentration greater than 40 μM at temperatures between about 30°C and about 40°C for a time between 50-200 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations. (see 0035,0036 and 0037).

Johnson discloses disclose a method of staining sperm cells comprising staining sperm cells with a staining mixture comprising Hoechst 33342, i.e. a DNA fluorescent dye, at a concentrations ranging from 4-5μg/ml at temperatures between about 30°C and about 39°C for a time between 60-120 minutes, and further disclose optimizing these parameters by adjusting time, temperature and dye concentrations (see column 4, lines 27-44).

Neither Seidel or Johnson teach the staining mixture to contain a composition which regulates oxidation/reduction reactions such as Vitamin K and lipoic acid.

However, Remington discloses the use of Vitamin K and lipoamide, i.e, lipoic acid, to study redox reactions intracellularly (see col. 15,16).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have added vitamin K and/or lipoic acid to a composition as oxidation/reduction agents because they are known oxidation/reduction agents because of their ability to donate and accept electrons.

One of ordinary skill in the art would have been motivated to add a redox agent such as Vitamin K or lipoic acid because Remington teaches both as redox agents used intracellularly . One would reasonably have expected success in Vitamin K or lipoic acid because they are disclosed in the art as acceptable redox agents.

Although the concentrations and temperatures claimed by applicant are not disclosed in the art, it would have been obvious to one of ordinary skill in the art at the time of the invention to adjust the process and buffer components to a concentrations

and temperatures optimal for such invention, therefore optimizing these result effective variables is the result of routine experimentation.

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference

process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."). See MPEP 2144.05.

Thus ,the claimed invention as a whole is prima facie obvious over the prior art.

Conclusion

No claims are found allowable

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tiffany M. Gough whose telephone number is 571-272-0697. The examiner can normally be reached on M-F 8-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

tmg

RUTH DAVIS
PRIMARY EXAMINER